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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/779,595	02/13/2004	Xianqiang Li	26757-702.301	8346

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/779,595	LI, XIANQIANG	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-36 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-36 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 13 February 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-36 are pending and under examination.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide an adequate description of the claimed method of identifying which of a plurality of different activated transcription factors are present in a biological sample. The disclosure presents general teachings relating to the picking of the individual components that can be employed in the method. However, not a single library of DNA probes has been made or the kind of library that would be suited to the practice of the invention. Likewise, there is no process step as how the recognition sequence in the library is varying within the library. Furthermore, the specification fails to teach a single activated transcription factor that forms a complex with the tf probe(s), let alone, the innumerable activated tf present in a biological sample. Neither was there a single biological sample given to show the presence of a single activated tf and/or the numerous, undefined, unknown different activated transcription factors present therein. This is made more compelling because not a single working example has been provided to direct a skilled artisan to the practice of the huge scope of the claimed invention. As stated by Li et al (US 2002/01686400) at page 8, [0107] ".. it is important to

understand that in any library system encoded by oligonucleotide synthesis one cannot have complete control over the codons that will eventually be incorporated into the peptide structure. This is especially true in the case of codons encoding stop signs…" Due to the high level of DNA binding specificity of transcription factors, each transcription factor will typically bind to a different DNA sequence. In some instances, a related family of transcription factors may bind to the same DNA sequence. Selection of the sequences used in the hybridization probes may be based on the different tfs that one wishes to detect in a sample. This in turn may depend on the type of organism, cell, or disease state one wished to identify and/or monitor the gene expression of. It is noted that different organisms will also express different activated transcription factors and the expression level could be biased. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(

1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993) [The claims at issued in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)]. There is no guidance or direction in selecting compounds to test or provide information that would narrow wide range of possible compounds. University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite as to step by which the recognition sequences would differentiate one cell to be malignant from the benign and normal cells.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-24 and 26-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhu et al [USP 6,410,246 (I) or 6,406,863(II)].

Zhu discloses at col. 6, line 62 up col. 9, line 45 a method for selecting tester proteins (activated

transcription factors, as claimed) capable of binding to a target peptide comprising expressing a library of tester proteins in yeast cells, each tester protein being a fusion protein comprised of a first polypeptide subunit whose sequence varies within the library, a second polypeptide subunit whose sequence varies within the library independently of the first polypeptide, and a linker peptide which links the first and second polypeptide subunits; expressing one or more target fusion proteins in the yeast cells expressing the tester proteins, each of the target fusion proteins comprising a target peptide or protein; and selecting those yeast cells in which a reporter gene is expressed, the expression of the reporter gene being activated by binding of the tester fusion protein to the target fusion protein. According to this embodiment, expression of the reporter gene may be activated by a functional transcription activator being formed by the binding of the tester protein to the target peptide or protein as in a yeast two-hybrid system. Also according to this variation, members of the library of tester expression vectors may be arrayed as individual yeast clones in one or more multiple-well plates.

Also according to this variation, the plurality of the target expression vectors may be arrayed as individual yeast clones in one or more multiple-well plates.

In any of the above-described methods for selecting tester proteins capable of binding to a target peptide, protein, or DNA, the method may further comprise isolating the tester expression vectors from the selected yeast cells; and mutagenizing the first and second nucleotide sequences in the isolated tester expression vectors to form a library of mutagenized expression vectors. Zhu discloses at col. 24, line62 up to col. 25, line 26 that the target protein may also be a mutated tumor suppressor gene. Examples of the tumor suppressor genes include, but are not limited to, DPC-4, NF-1, NF-2, RB, p53, WT1, BRCA1 and BRCA2. See specifically the Examples. Zhu (II) basically discloses the same method as Zhu (I) above. See the claims. Accordingly, the specific method steps of Zhu (I or II) anticipates the broad claimed method.

Claims 1-2, 18, 19,22 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Weissman et al (US 6,066,452).

Weismann et al discloses at col. 2, line 17 up to col.3, line 25 a method comprising: (a) mixing a set of oligonucleotide

duplexes comprising 5' and 3' sequences that will hybridize to primers for amplification and an internal sequence of random nucleotides, and a sample containing a mixture of DNA-binding proteins (activated transcription factors, as claimed); (b) separating unbound oligonucleotide duplexes from oligonucleotide duplexes complexed with the DNA-binding proteins on the basis of differences in physical or biochemical properties; (c) recovering the DNA-binding proteins from the complexes. Subsequent to step (b): the complexed duplexes are amplified, mixed with the sample containing DNA-binding proteins; and separated on the basis of differences in physical or biochemical properties; wherein the amplifying, mixing, and separating steps are performed one or more times. The sample is a nuclear extract, a cellular extract or intact nuclei. The internal sequence is a random 12 sequence, from about 6 to about 25 base pairs or is from about 8 to about 12 base pairs. The method of separation is based on differences in mobility, such as polyacrylamide gel electrophoresis or size-exclusion chromatography. In another embodiment Weissman discloses a method for simultaneously determining nucleotide recognition sequences for DNA-binding proteins, comprising the steps outlined above, further comprising analyzing the amplified duplexes to determine nucleotide recognition sequences for the

DNA-binding proteins. The analyzing step comprises ligating the amplified duplexes to a vector to generate clones; and determining the DNA sequences of the cloned duplexes. The analyzing step comprises denaturing the amplified duplexes; hybridizing the denatured duplexes to an array of single-stranded oligonucleotides having different sequences; and detecting oligonucleotides hybridized with denatured duplexes. See further col. 4, line 12 as to the multiple selection technique up to col. 18, line 60, including the Examples. The Examples provide a detailed description of the method utilizing specific process steps with specific components. Examples 3 and 4 recite the various combinations of transcription factors that have been identified e.g., Pit-1 and ANF. It is considered that internal sequence of a random 12 sequence, from about 6 to about 25 base pairs reads on the claimed transcription factor probes wherein the recognition sequence varies within the library. The transcription factor probes of Weismann is also a known probe wherein recognition sequence is randomized i.e., varied, as claimed. The specific process steps of Weissman therefore fully meet the broad claimed process of undefined components therein.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states "whoever invents or discovers any new

and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 25 and 35 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 6,696,256 ('256 Patent) or provisionally rejected over claim 1 of copending application 09/877,403 ('403 application). This is a double patenting rejection.

The instant claimed method is identical or else are so close in content with the '256 Patent and '403 application that they both cover the same thing. These claims recite the same method of identifying a plurality of different activated transcription factors or individual transcription factor in a biological sample as the instant claims.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-20, 22-34 and 36 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 and 22 of copending Application No. 09/877,403 ('403) or over claims 1-19 of Patent No. 6,696,256 ('256 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because are nearly identical method claims except in the preamble. The instant claimed method using broadly a known recognition sequence that varies within the library encompasses the specific known transcription factors binding recognition sequence recited in the '256 Patent or the '403 application. See the instant disclosure.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D.

Wessendorf whose telephone number is (571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
September 30, 2004